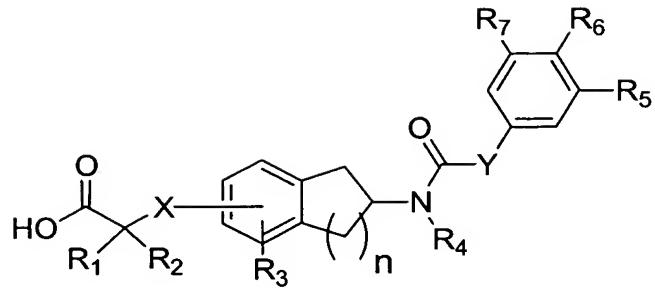


CLAIMS

1. A compound of Formula I

5



Formula I

or a pharmaceutically acceptable salt, C₁₋₆ ester or C₁₋₆ amide thereof, wherein

10

each of R₁ and R₂ is independently H, C₁₋₆ alkyl, (CH₂)_mNR_aR_b, (CH₂)_mOR₈, (CH₂)_mNH(CO)R₈, or (CH₂)_mCO₂R₈, where each of R_a, R_b, and R₈ is independently H or C₁₋₆ alkyl, or R₁ and R₂ taken together with the carbon atom to which they are attached are a C₃₋₇ cycloalkyl;

15

m is between 1 and 6;

n is 1 or 2;

X is O or S; wherein X is at the 5 or 6 position when n is 1; and wherein X is at 20 the 6 or 7 position when n is 2;

R₃ is H, phenyl, C₁₋₃ alkoxy, C₁₋₃ alkylthio, halo, cyano, C₁₋₆ alkyl, nitro, NR₉R₁₀, NHCOR₁₀, CONHR₁₀; and COOR₁₀; and R₃ is ortho or meta to X;

25 R₄ is H or -(C₁₋₅ alkylene)R₁₅, where R₁₅ is H, C₁₋₇ alkyl, [di(C₁₋₂ alkyl)amino](C₁₋₆ alkylene), (C₁₋₃ alkoxyacetyl)(C₁₋₆ alkylene), C₁₋₆ alkoxy, C₃₋₇ alkenyl, or C₃₋₈ alkynyl, wherein R₄ has no more than 9 carbon atoms; R₄ can

also be -(C₁₋₅ alkylene)R₁₅ wherein R₁₅ is C₃₋₆ cycloalkyl, phenyl, phenyl-O-, phenyl-S-, or a 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

5 Y is NH, NH-CH₂, and O;

each of R₅ and R₇ is independently selected from H, C₁₋₆ alkyl, halo, cyano, nitro, COR₁₁, COOR₁₁, C₁₋₄ alkoxy, C₁₋₄ alkylthio, hydroxy, phenyl, NR₁₁R₁₂ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected
10 from N, O, and S;

R₆ is selected from C₁₋₆ alkyl, halo, cyano, nitro, COR₁₃, COOR₁₃, C₁₋₄ alkoxy, C₁₋₄ alkylthio, hydroxy, phenyl, NR₁₃R₁₄ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

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in addition, either R₅ and R₆ or R₆ and R₇ may be taken together to be a bivalent moiety, saturated or unsaturated, selected from -(CH₂)₃-, -(CH₂)₄-, and (CH₁₋₂)_pN(CH₁₋₂)_q,

20

p is 0-2 and q is 1-3, where the sum (p + q) is at least 2;

each of R₉ and R₁₀ is independently C₁₋₆ alkyl;

each of R₁₁, R₁₂, R₁₃ and R₁₄ is independently H or C₁₋₆ alkyl;

25

wherein each of the above hydrocarbyl and heterocarbyl moieties may be substituted with between 1 and 3 substituents independently selected from F, Cl, Br, I, amino, methyl, ethyl, hydroxy, nitro, cyano, and methoxy.

2. A compound of claim 1, wherein one of R₁ and R₂ is methyl or ethyl.

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3. A compound of claim 2, wherein each of R₁ and R₂ is methyl.

4. A compound of claim 1, wherein R₁ and R₂ taken together are cyclobutyl or cyclopentyl.

5 5. A compound of claim 1, wherein R₃ is H.

6. A compound of claim 1, wherein R₃ is C₁₋₃ alkoxy, C₁₋₃ alkylthio, halo, cyano, C₁₋₆ alkyl, nitro, NR₉R₁₀, NHCOR₁₀, CONHR₁₀; or COOR₁₀.

10 7. A compound of claim 1, wherein R₄ is H or C₂₋₇ alkyl.

8. A compound of claim 7, wherein R₄ is H or C₂₋₅ alkyl.

9. A compound of claim 8, wherein R₄ is ethyl.

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10. A compound of claim 8, wherein R₄ is H.

11. A compound of claim 1, wherein n is 1.

20 12. A compound of claim 1, wherein n is 2.

13. A compound of claim 1, wherein Y is NH-CH₂.

14. A compound of claim 1, wherein Y is NH.

25

15. A compound of claim 1, wherein X is S.

16. A compound of claim 1, wherein X is O.

30 17. A compound of claim 1, wherein at least one of R₅ and R₇ is H.

18. A compound of claim 17, wherein R₆ is C₁₋₄ alkyl, halomethoxy, halomethylthio, or di(C₁₋₃ alkyl)amino.

19. A compound of claim 18, wherein R₆ is trifluoromethoxy, difluoromethoxy, 5 trifluoromethyl, trifluoromethylthio, t-butyl, isopropyl, or dimethylamino.

20. A compound of claim 3, wherein R₃ is H, R₄ is C₂₋₇ alkyl, and Y is NH.

21. A compound of claim 20, wherein X is S.

10

22. A compound of claim 20, wherein n is 1.

23. A compound of claim 20, wherein n is 2.

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24. A compound of claim 20, wherein R₄ is C₂₋₅ alkyl.

25. A compound of claim 24, wherein R₄ is ethyl.

26. A compound of claim 20, wherein R₆ is trifluoromethoxy, difluoromethoxy, trifluoromethyl, trifluoromethylthio, t-butyl, isopropyl, or dimethylamino.

27. A compound of claim 1, wherein each of R₁ and R₂ is independently H, C₁₋₆ alkyl, (CH₂)_mNR_aR_b, or (CH₂)_mOR₈, where each of R_a, R_b, and R₈ is independently H or C₁₋₆ alkyl;

25

m is between 1 and 6;

n is 1 or 2;

X is O or S; wherein X is at the 5 or 6 position when n is 1; and wherein X is at 30 the 6 or 7 position when n is 2;

R_3 is H, phenyl, C₁₋₃ alkoxy, C₁₋₃ alkylthio, halo, C₁₋₆ alkyl, or NR₉R₁₀, and R₃ is ortho or meta to X;

5 R₄ is H or -(C₁₋₅ alkylene)R₁₅, where R₁₅ is H, C₁₋₇ alkyl, [di(C₁₋₂ alkyl)amino](C₁₋₆ alkylene), (C₁₋₃ alkoxyacyl)(C₁₋₆ alkylene), C₁₋₆ alkoxy, or C₃₋₇ alkenyl, wherein R₄ has no more than 9 carbon atoms;

10 R₄ can also be -(C₁₋₅ alkylene)R₁₅ wherein R₁₅ is C₃₋₆ cycloalkyl, phenyl, phenyl-O-, phenyl-S-, or a 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

15 Y is NH or NHCH₂;

each of R₅ and R₇ is independently selected from H, C₁₋₆ alkyl, halo, COR₁₁, COOR₁₁, C₁₋₄ alkoxy, C₁₋₄ alkylthio, hydroxy, and NR₁₁R₁₂;

20 R₆ is selected from C₁₋₆ alkyl, halo, COR₁₃, COOR₁₃, C₁₋₄ alkoxy, C₁₋₄ alkylthio, phenyl, NR₁₃R₁₄ and 5-6 membered heterocyclyl with between 1 and 2 heteroatoms selected from N, O, and S;

25 each of R₉ and R₁₀ is independently C₁₋₆ alkyl;

each of R₁₁, R₁₂, R₁₃ and R₁₄ is independently H or C₁₋₆ alkyl;

wherein each of the above hydrocarbyl and heterocarbyl moieties may be substituted with between 1 and 3 substituents independently selected from F, Cl, amino, methyl, ethyl, hydroxy, and methoxy.

28. A compound of claim 1, selected from:

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

30 2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-pentyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

5 2-{2-[1-Ethyl-3-(4-isopropylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-pentyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

10 2-{2-[3-(4-Dimethylaminophenyl)-1-ethylureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-Methyl-2-{2-[1-(3-methylbutyl)-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-methylbutyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

15 2-Methy-2-{2-[1-pent-4-enyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

20 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-chloro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-bromo-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

25 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid; and

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-trifluoromethoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid.

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29. A compound of claim 1, selected from

2-Methyl-2-{2-[1-hexyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid ;

2-{2-[3-(4-Dimethylaminophenyl)-1-pentylureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

5 2-Methyl-2-{2-[3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

10 2-Methyl-2-{2-[1-butyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-pentyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

2-{2-[3-(4-*tert*-Butylphenyl)-1-(3-pentyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

15 2-[2-(3-(Biphenyl-4-yl-1-pentylureido)indan-5-ylsulfanyl]-2-methylpropionic acid;

2-{2-[3-(4-Isopropylphenyl)-1-(3-hexyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;

20 2-Methyl-2-{2-[1-butyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methoxy-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

25 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-chloro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-bromo-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;

30 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid; and

2-Methyl-2-{2-[1-hexyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid.

30. A compound of claim 1, selected from:

5 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;
10 2-{6-[3-(4-Trifluoromethoxyphenyl)ureido]-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;
15 2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;
20 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;
25 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-methyl-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid;
30 2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid; and
35 2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid.

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31. A compound of claim 1, selected from:

2-{2-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;
25 2-{2-[1-Ethyl-3-(4-trifluoromethylsulfanylphenyl)ureido]indan-5-ylsulfanyl}-2-methylpropionic acid;
30 2-Methyl-2-{2-[1-propyl-3-(4-trifluoromethoxyphenyl)ureido]indan-5-ylsulfanyl}propionic acid; and
35 2-{6-[1-Ethyl-3-(4-trifluoromethoxyphenyl)ureido]-3-fluoro-5,6,7,8-tetrahydronaphthalen-2-ylsulfanyl}-2-methylpropionic acid.

30

32. A pharmaceutical composition, comprising a compound of claim 1, 20, 27, 28, 30, or 31.

33. A method for treating or inhibiting the progression of Syndrome X, said
5 method comprising administering to a patient in need of treatment a
pharmaceutically-effective amount of a composition comprising a compound
of claim 1, 20, 27, 28 or 31.

34. A method of claim 33, wherein said Syndrome X is a combination of
10 (a) One or more conditions selected from impaired glucose tolerance,
hyperinsulinemia, hyperglycemia, insulin resistance, and early,
intermediate or late Type II diabetes (NIDDM), impaired fasting glucose
tolerance, and complications thereof;
(b) Dyslipidemia
15 (c) Obesity or an overweight condition; and
(d) Hypertension.

35. A method of claim 33, wherein said Syndrome X is a combination of two or
more conditions selected from (a).

20 36. A method of claim 33, wherein said compound is a first pharmaceutically
active agent, and wherein said method further comprises the step of
administering to the patient a jointly-effective amount of a second
pharmaceutically active agent that is an anti-diabetic agent, a lipid lowering
25 agent, or a blood-pressure lowering agent.

37. A method of claim 36, wherein said second agent is selected from insulin
and PPAR alpha or PPAR gamma modulating agents.

30 38. A method of claim 36, further comprising the step of administering a jointly-
effective amount of a third pharmaceutically active agent.

39. A method of claim 39, wherein said third pharmaceutically active agent is selected from an anti-diabetic agent, a lipid lowering agent, and a blood-pressure lowering agent.

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40. A method for treating obesity or an overweight condition, said method comprising the step of administering to a patient a pharmaceutically effective amount of a composition comprising a compound of formula (I).

10 41. A method of claim 40, wherein said method is a method for treating dyslipidemia and either obesity or an overweight condition.

42. A method of claim 40, wherein said method is a method for treating obesity and a condition selected from Type II diabetes, insulin resistance, hyperglycemia, impaired glucose tolerance, and hyperinsulinemia.

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